

## Complete if Known

INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT

(Use as many sheets as necessary)

Sheet

1

of

6

Application Number	10/669,217
Filing Date	September 23, 2003
First Named Inventor	Robert W. ESMOND
Art Unit	1618
Examiner Name	Vickie Y. Kim
Attorney Docket Number	4012.0373-02000

## U.S. PATENTS AND PUBLISHED U.S. PATENT APPLICATIONS

Examiner Initials	Cite No. <sup>1</sup>	Document Number Number-Kind Code <sup>2</sup> (if known)	Issue or Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear

Note: Submission of copies of U.S. Patents and published U.S. Patent Applications is not required.

## FOREIGN PATENT DOCUMENTS

Examiner Initials	Cite No. <sup>1</sup>	Foreign Patent Document Country Code <sup>3</sup> Number <sup>4</sup> Kind Code <sup>5</sup> (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	Translation <sup>6</sup>

## NON PATENT LITERATURE DOCUMENTS

Examiner Initials	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	Translation <sup>8</sup>
		Roses, Allen D., patent application filed on September 22, 2005, at the U.S. Patent and Trademark Office for "Novel Method."	
		Alessi et al., "The role of PI 3-kinase in insulin action," <i>Biochim. Biophys. Acta</i> , 1436:151-164 (1998).	
		Beal et al., "Somatostatin: alterations in the central nervous system in neurological diseases," <i>Res. Publ. Assoc. Res. Nerv. Ment. Dis.</i> , 64: 215-257 (1986).	
		Bernstein et al., "Insulin-degrading enzyme in the Alzheimer's disease brain: prominent localization in neurons and senile plaques," <i>Neurosci. Lett.</i> , 263: 161-164 (1999).	
		Bertram et al., "Evidence for genetic linkage of Alzheimer's disease to chromosome 10q," <i>Science</i> , 290: 2302-2303 (2000).	
		Braak et al., "Diagnostic criteria for neuropathologic assessment of Alzheimer's disease," <i>Neurobiol. Aging</i> , 18: S85-S88 (1997).	
		Brunet et al., "Akt promotes cell survival by phosphorylating and inhibiting a Forkhead transcription factor," <i>Cell</i> , 96: 857-868 (1999).	
		Bucht et al., "Changes in blood glucose and insulin secretion in patients with senile dementia of Alzheimer type," <i>Acta Med. Scand.</i> , 213: 387-392 (1983).	
		Burgering et al., "Protein kinase B (c-Akt) in phosphatidylinositol-3-OH kinase signal transduction," <i>Nature</i> , 376: 599-602 (1995).	
		Carantoni et al., "Alzheimer disease and vascular dementia: relationships with fasting glucose and insulin levels," <i>Dement. Geriatr. Cogn. Discard.</i> , 11: 176-180 (2000).	
		Carson et al., "Insulin-like growth factor I increases brain growth and central nervous system myelination in transgenic mice," <i>Neuron</i> , 10: 729-740 (1993).	
		Connor et al., "Insulin-like growth factor-I (IGF-I) immunoreactivity in the Alzheimer's disease temporal cortex and hippocampus," <i>Mol. Brain Res.</i> , 49: 283-290 (1997).	
		Craft et al., "Insulin effects on glucose metabolism, memory and plasma amyloid precursor protein in Alzheimer's disease differ according to apolipoprotein-E genotype," <i>Ann. NY Acad. Sci.</i> , 903: 222-228 (2000).	
		Craft et al., "Enhancement of memory in Alzheimer disease with insulin and somatostatin, but not glucose," <i>Arch. Gen. Psychiatry</i> , 56: 1135-1140 (1999).	
		Craft et al., "Insulin metabolism in Alzheimer's disease differs according to apolipoprotein E genotype and gender," <i>Neuroendocrinology</i> , 70: 146-152 (1999).	

CERTIFICATE UNDER 37 CFR § 1.10 OF MAILING BY "EXPRESS MAIL"

EV 398887974 US

November 17, 2005

USPS Express Mail Label Number

Date of Deposit

I hereby certify that this correspondence is being deposited with the United States Postal Service "Express Mail Post Office to Addressee" service under 37 CFR § 1.10 on the date indicated above and is addressed to Mail Stop Agreement, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

By:

Nancy Foster

2/1/06

IDS Form PTO/SB/08: Substitute for form 1449A/PTO				<b>Complete if Known</b>	
<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>  (Use as many sheets as necessary)				Application Number	10/669,217
				Filing Date	September 23, 2003
				First Named Inventor	Robert W. ESMOND
				Art Unit	1618
				Examiner Name	Vickie Y. Kim
Sheet	2	of	6	Attorney Docket Number	4012.0373-02000

	Crews et al., "Binding of [ <sup>125</sup> I]-insulin-like growth factor-1 (IGF-1) in brains of Alzheimer's and alcoholic patients," <i>Adv. Exp. Med. Biol.</i> , 293: 483-492 (1991).	
	Crews et al., "Insulin-like growth factor I receptor binding in brains of Alzheimer's and alcoholic patients," <i>J. Neurochem.</i> , 58: 1205-1210 (1992).	
	D'Ercole et al., "The role of the insulin-like growth factors in the central nervous system," <i>Mol. Neurobiol.</i> , 13: 227-255 (1996).	
	D'Ercole et al., "Use of transgenic mice for understanding the physiology of insulin-like growth factors," <i>Horm. Res.</i> , 45 (Supp.1): 5-7 (1996).	
	D'Ercole, A., "Expression of insulin-like growth factor-I in transgenic mice," <i>Ann. NY Acad. Sci.</i> , 692: 149-160 (1993).	
	da Silva et al., "Quantitative evaluation of the rRNA in Alzheimer's disease," <i>Mech. Ageing Dev.</i> , 120: 57-64 (2000).	
	Datta et al., "Akt phosphorylation of BAD couples survival signals to the cell-intrinsic death machinery," <i>Cell</i> , 91: 231-241 (1997).	
	De Ferrari et al., "Wnt signaling function in Alzheimer's disease," <i>Brain Res. Rev.</i> , 33: 1-12 (2000).	
	De Keyser et al., "Insulin-like growth factor-I receptor densities in human frontal cortex and white matter during aging, in Alzheimer's disease, and in Huntington's disease," <i>Neurosci. Lett.</i> , 172: 93-96 (1994).	
	de la Monte et al., "Partial rescue of ethanol-induced neuronal apoptosis by growth factor activation of phosphoinositol-3-kinase," <i>Alcohol. Clin. Exp. Res.</i> , 24: 716-726 (2000).	
	de la Monte et al., "Mitochondrial DNA damage as a mechanism of cell loss in Alzheimer's disease," <i>Lab Invest.</i> , 80: 1323-1335 (2000).	
	de la Monte et al., "Oxygen free radical injury is sufficient to cause some Alzheimer-type molecular abnormalities in human CNS neuronal cells," <i>J. Alzheimer's Dis.</i> , 2: 261-281 (2000).	
	de la Torre, J., "Critically attained threshold of cerebral hypoperfusion: the CATCH hypothesis of Alzheimer's pathogenesis," <i>Neurobiol. Aging</i> , 21: 331-342 (2000).	
	Delcommenne et al., "Phosphoinositide-3-OH kinase-dependent regulation of glycogen synthase kinase 3 and protein kinase B/AKT by the integrin-linked kinase," <i>Proc. Natl. Acad. Sci. USA</i> , 95: 11211-11216 (1998).	
	Dentremont et al., "Increased insulin-like growth factor-I (IGF-I) expression during early postnatal development differentially increases neuron number and growth in medullary nuclei of the mouse," <i>Dev. Brain Res.</i> , 114: 135-141 (1999).	
	Doré et al., "Insulin-like growth factor I protects and rescues hippocampal neurons against $\beta$ -amyloid- and human amylin-induced toxicity," <i>Proc. Natl. Acad. Sci., USA</i> , 94: 4772-4777 (1997).	
	Doré et al., "Protective and rescuing abilities of IGF-I and some putative free radical scavengers against $\beta$ -amyloid-inducing toxicity in neurons," <i>Ann. NY Acad. Sci.</i> , 890: 356-364 (1999).	
	Doublier et al., "Impaired brain development and hydrocephalus in a line of transgenic mice with liver-specific expression of human Insulin-like growth factor binding protein-1," <i>Growth Horm. IGF Res.</i> , 10: 267-274 (2000).	
	Dudek et al., "Regulation of neuronal survival by the serine-threonine protein kinase Akt," <i>Science</i> , 275: 661-665 (1997).	
	Etiene et al., "Cerebrovascular pathology contributes to the heterogeneity of Alzheimer's disease," <i>J. Alzheimer's Dis.</i> , 1: 119-134 (1998).	
	Eyes et al., "Akt, a target of phosphatidylinositol 3-kinase, inhibits apoptosis in a differentiating neuronal cell line," <i>Mol. Cell Biol.</i> , 18: 2143-2152 (1998).	
	Fisman et al., "Metabolic changes in Alzheimer's disease," <i>J. Am. Geriatr. Soc.</i> , 36: 298-300 (1988).	
	Folli et al., "The early intracellular signaling pathway for the insulin/insulin-like growth factor receptor family in the mammalian central nervous system," <i>Mol. Neurobiol.</i> , 13: 155-183 (1996).	

 2/1/06

IDS Form PTO/SB/08: Substitute for form 1449A/PTO				<b>Complete if Known</b>	
<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>  (Use as many sheets as necessary)				Application Number	10/669,217
				Filing Date	September 23, 2003
				First Named Inventor	Robert W. ESMOND
				Art Unit	1618
				Examiner Name	Vickie Y. Kim
Sheet	3	of	6	Attorney Docket Number	4012.0373-02000

19	Frölich et al., "Brain insulin and insulin receptors in aging and sporadic Alzheimer's disease," <i>J. Neural Transm.</i> , 105: 423-438 (1998).	
	Frölich et al., "A disturbance in the neuronal insulin receptor signal transduction in sporadic Alzheimer's disease," <i>Ann. NY Acad. Sci.</i> , 893: 290-293 (1999).	
	Fujisawa et al., "Increased insulin levels after OGTT load in peripheral blood and cerebrospinal fluid of patients with dementia of Alzheimer type," <i>Biol. Psychiatry</i> , 30: 1219-1228 (1991).	
	Garver et al., "Tau phosphorylation in brain slices: pharmacological evidence for convergent effects of protein phosphatases on tau and mitogen-activated protein kinase," <i>Mol. Pharmacol.</i> , 47: 745-756 (1995).	
	Giovannone et al., "Insulin receptor substrate (IRS) transduction system: distinct and overlapping signaling potential," <i>Diabetes Metab. Res. Rev.</i> , 16: 434-441 (2000).	
	Glenner et al., "Alzheimer's disease: initial report of the purification and characterization of a novel cerebrovascular amyloid protein," <i>Biochem. Biophys. Res. Commun.</i> , 120: 885-890 (1984).	
	Halestrap et al., "Mitochondria and cell death," <i>Biochem. Soc. Trans.</i> , 28: 170-177 (2000).	
	Heidenreich et al., "Insulin receptors mediate growth effects in cultured fetal neurons. I. Rapid stimulation of protein synthesis," <i>Endocrinology</i> , 125: 1451-1457 (1989).	
	Hetman et al., "Role of glycogen synthase kinase-3 $\beta$ in neuronal apoptosis induced by trophic withdrawal," <i>J. Neurosci.</i> , 20: 2567-2574 (2000).	
	Hirsch et al., "Mitochondrial permeability transition in apoptosis and necrosis," <i>Cell Biol. Toxicol.</i> , 14: 141-145 (1998).	
	Hong et al., "Insulin and insulin-like growth factor-1 regulate tau phosphorylation in cultured human neurons," <i>J. Biol. Chem.</i> , 272: 19547-19553 (1997).	
	Hoyer et al., "Inhibition of the neuronal insulin receptor: An in vivo model for sporadic Alzheimer disease?," <i>Ann. NY Acad. Sci.</i> , 920: 256-258 (2000).	
	Hoyer et al., "Inhibition of the neuronal insulin receptor causes Alzheimer-like disturbances in oxidative/energy brain metabolism and in behavior in adult rats," <i>Ann. NY Acad. Sci. USA</i> , 893: 301-303 (1999).	
	Hoyer et al., "Predominant abnormality in cerebral glucose utilization in late-onset dementia of the Alzheimer type: a cross-sectional comparison against advanced late-onset and incipient early-onset cases," <i>J. Neural Transm. [P-D Sect]</i> , 3: 1-14 (1991).	
	Hoyer et al., "Cerebral excess release of neurotransmitter amino acids subsequent to reduced cerebral glucose metabolism in early-onset dementia of Alzheimer type," <i>J. Neural Transm.</i> , 75: 227-232 (1989).	
	Hoyer et al., "Desensitization of brain insulin receptor: Effect on glucose/energy and related metabolism," <i>J. Neural Transm., Supp</i> 44: 259-268 (1994).	
	Hoyer, S., "Somatostatin and Alzheimer's disease," <i>J. Neurol.</i> , 234: 266-267 (1987).	
	Hoyer, S., "Brain glucose and energy metabolism abnormalities in sporadic Alzheimer disease. Causes and consequences: an update," <i>Exp. Gerontol.</i> , 35: 1363-1372 (2000).	
	Hoyer, S., "Age as risk factor for sporadic dementia of the Alzheimer type?," <i>Ann. NY Acad. Sci.</i> , 719: 248-256 (1994).	
	Hoyer, S., "Neurodegeneration, Alzheimer's disease, and beta-amyloid toxicity," <i>Life Sci.</i> , 55: 1977-1983 (1994).	
	Hoyer, S., "Oxidative metabolism deficiencies in brains of patients with Alzheimer's disease," <i>Acta Neurol. Scand., Suppl.</i> 165: 18-24 (1996).	
be	Jafferall et al., "Insulin-like growth factor-I and its receptor in the frontal cortex, hippocampus, and cerebellum of normal human and alzheimer disease brains," <i>Synapse</i> , 38: 450-459 (2000).	

*[Handwritten signature]* 2/1/06

**INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT**

(Use as many sheets as necessary)

Sheet

4

of

6

**Complete if Known**

Application Number	10/669,217
Filing Date	September 23, 2003
First Named Inventor	Robert W. ESMOND
Art Unit	1618
Examiner Name	Vickie Y. Kim
Attorney Docket Number	4012.0373-02000

	Kennedy et al., "Akt/protein kinase B inhibits cell death by preventing the release of cytochrome c from mitochondria," <i>Mol. Cell. Biol.</i> , 19: 5800-5810 (1999).	
	Kulik et al., "Antiapoptotic signalling by the insulin-like growth factor I receptor, phosphatidylinositol 3-kinase, and Akt," <i>Mol. Cell. Biol.</i> , 17: 1595-1606 (1997).	
	Lam et al., "The phosphatidylinositol 3-kinase serine kinase phosphorylates IRS-1. Stimulation by insulin and inhibition by Wortmannin," <i>J. Biol. Chem.</i> , 269: 20648-20652 (1994).	
	Lannert et al., "Intracerebroventricular administration of streptozotocin causes long-term diminutions in learning and memory abilities and in cerebral energy metabolism in adult rats," <i>Behav. Neurosci.</i> , 112: 1199-1208 (1998).	
	Lorenzo et al., "Amyloid fibril toxicity in Alzheimer's disease and diabetes," <i>Ann. NY Acad. Sci.</i> , 777: 89-95 (1996).	
	Lovestone et al., "Alzheimer's disease-like phosphorylation of the microtubule-associated protein tau by glycogen synthase kinase-3 in transfected mammalian cells," <i>Curr. Biol.</i> , 4: 1077-1086 (1994).	
	Mauvais-Jarvis et al., "Understanding the pathogenesis and treatment of insulin resistance and type 2 diabetes mellitus: what can we learn from transgenic and knockout mice?," <i>Diabetes Metab.</i> , 26: 433-448 (2000).	
	McDermott et al., "Degradation of Alzheimer's $\beta$ -amyloid protein by human and rat brain peptidases: involvement of insulin-degrading enzyme," <i>Neurochem Res.</i> , 22: 49-56 (1997).	
	Meneilly et al., "Alterations in glucose metabolism in patients with Alzheimer's disease," <i>J. Am. Geriatr. Soc.</i> , 41: 710-714 (1993).	
	Messier et al., "Glucose regulation and cognitive functions: relation to Alzheimer's disease and diabetes," <i>Behav. Brain Res.</i> , 75: 1-11 (1996).	
	Mill et al., "Insulin, insulin-like growth factor II, and nerve growth factor effects on tubulin mRNA levels and neurite formation," <i>Proc. Natl. Acad. Sci. USA</i> , 82: 7126-7130 (1985).	
	Moroo et al., "Loss of insulin receptor immunoreactivity from the substantia nigra pars compacta neurons in Parkinson's disease," <i>Acta Neuropathol.</i> , 87: 343-348 (1994).	
	Mustafa et al., "Decreased plasma insulin-like growth factor-I level in familial Alzheimer's disease patients carrying the Swedish APP 670/671 mutation," <i>Dement. Geriatr. Cogn. Disord.</i> , 10: 446-451 (1999).	
	Myers et al., "The IRS-1 signaling system," <i>Trends Biochem. Sci.</i> , 19: 289-293 (1994).	
	Nagy et al., "Assessment of the pathological stages of Alzheimer's disease in thin paraffin sections: a comparative study," <i>Dement. Geriatr. Cogn. Disord.</i> , 9: 140-144 (1998).	
	Ni et al., "Impaired brain development and reduced astrocyte response to injury in transgenic mice expressing IGF binding protein-1," <i>Brain Res.</i> , 769: 97-107 (1997).	
	Nilni et al., "Identification of the thyrotropin-releasing hormone precursor, its processing products, and its coexpression with convertase 1 in primary cultures of hypothalamic neurons: anatomic distribution of PC1 and PC2," <i>Endocrinology</i> , 137: 5651-5661 (1996).	
	Nishimura et al., "Presenilin mutations associated with Alzheimer disease cause defective intracellular trafficking of $\beta$ -catenin, a component of the presenilin protein complex," <i>Nat. Med.</i> , 5: 164-169 (1999).	
	Nishiyama et al., "Expression of the gene encoding the tyrosine kinase-deficient human insulin receptor in transgenic mice," <i>Gene</i> , 141: 187-192 (1994).	
	O'Hare et al., "Intrinsic kinase activity of the insulin receptor," <i>Int. J. Biochem.</i> , 22: 315-324 (1990).	
	O'Kusky et al., "Insulin-like growth factor-I promotes neurogenesis and synaptogenesis in the hippocampal dentate gyrus during postnatal development," <i>J. Neurosci.</i> , 20: 8435-8442 (2000).	
	Ott et al., "Association of diabetes mellitus and dementia: the Rotterdam Study," <i>Diabetologia</i> , 39: 1392-1397 (1996).	

**INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT**

(Use as many sheets as necessary)

Sheet

5

of

6

**Complete if Known**

Application Number	10/669,217
Filing Date	September 23, 2003
First Named Inventor	Robert W. ESMOND
Art Unit	1618
Examiner Name	Vickie Y. Kim
Attorney Docket Number	4012.0373-02000

	Ott et al., "Diabetes mellitus and the risk of dementia: The Rotterdam Study," <i>Neurology</i> , 53: 1937-1942 (1999).	
	Pap et al., "Role of glycogen synthase kinase-3 in the phosphatidylinositol 3-kinase/Akt cell survival pathway," <i>J. Biol. Chem.</i> , 273: 19929-19932 (1998).	
	Pastorino et al., "The overexpression of Bax produces cell death upon induction of the mitochondrial permeability transition," <i>J. Biol. Chem.</i> , 273: 7770-7775 (1998).	
	Patrick et al., "Conversion of p35 to p25 deregulates Cdk5 activity and promotes neurodegeneration," <i>Nature</i> , 402, 615-622 (1999).	
	Payão et al., "Ribosomal RNA in Alzheimer's disease and ageing," <i>Mech. Ageing Dev.</i> , 105: 265-272 (1998).	
	Pei et al., "Accumulation of cyclin-dependent kinase 5 (cdk5) in neurons with early stages of Alzheimer's disease neurofibrillary degeneration," <i>Brain Res.</i> , 797: 267-277 (1998).	
	Pérez et al., "Degradation of soluble amyloid $\beta$ -peptides 1-40, 1-42, and the Dutch variant 1-40Q by insulin degrading enzyme from Alzheimer disease and control brains," <i>Neurochem. Res.</i> , 25: 247-255 (2000).	
	Pete et al., "Postnatal growth responses to insulin-like growth factor I in insulin receptor substrate-1-deficient mice," <i>Endocrinology</i> , 140: 5478-5487 (1999).	
	Plaschke et al., "Action of the diabetogenic drug streptozotocin on glycolytic and glycogenolytic metabolism in adult rat brain cortex and hippocampus," <i>Int. J. Dev. Neurosci.</i> , 11: 477-483 (1993).	
	Puro et al., "Insulin-mediated regulation of neuronal maturation," <i>Science</i> , 225: 1170-1172 (1984).	
	Qiu et al., "Insulin-degrading enzyme regulates extracellular levels of amyloid $\beta$ -protein by degradation," <i>J. Biol. Chem.</i> , 273: 32730-32738 (1998).	
	Reubi et al., "Somatostatin and Alzheimer's disease: a hypothesis," <i>J. Neurol.</i> , 233: 370-372 (1986).	
	Shpakov et al., "Structural and functional characterization of insulin receptor substrate proteins and the molecular mechanisms of their interaction with insulin superfamily tyrosine kinase receptors and effector proteins," <i>Membr. Cell Biol.</i> , 13: 455-484 (2000).	
	Smith et al., "Insulin signaling and action in fat cells: associations with insulin resistance and type 2 diabetes," <i>Ann. NY Acad. Sci.</i> , 892: 119-126 (1999).	
	Spindler et al., "Nutritional status of patients with Alzheimer's disease: a 1-year study," <i>J. Am. Diet Assoc.</i> , 96: 1013-1018 (1996).	
	Sun et al., "Structure of the insulin receptor substrate IRS-1 defines a unique signal transduction protein," <i>Nature</i> , 352: 73-77 (1991).	
	Sun et al., "Pleiotropic insulin signals are engaged by multisite phosphorylation of IRS-1," <i>Mol. Cell. Biol.</i> , 13: 7418-7428 (1993).	
	Tham et al., "Insulin-like growth factors and somatomedin B in the cerebrospinal fluid of patients with dementia of the Alzheimer type," <i>Acta Psychiatr. Scand.</i> , 77: 719-723 (1988).	
	Tham et al., "Insulin-like growth factors and insulin-like growth factor binding proteins in cerebrospinal fluid and serum of patients with dementia of the Alzheimer type," <i>J. Neural Transm. [P-D Sect.]</i> , 5: 165-176 (1993).	
	Ullrich et al., "Human insulin receptor and its relationship to the tyrosine kinase family of oncogenes," <i>Nature</i> , 313: 756-761 (1985).	
	Unger et al., "Insulin receptors in the central nervous system: localization, signalling mechanisms and functional aspects," <i>Prog. Neurobiol.</i> , 36: 343-362 (1991).	
	Unger et al., "Immunohistochemical localization of insulin receptors and phosphotyrosine in the brainstem of the adult rat," <i>Neuroscience</i> , 42: 853-861 (1991).	

2/1/06

IDS Form PTO/SB/08: Substitute for form 1449A/PTO				<b>Complete if Known</b>	
<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>  (Use as many sheets as necessary)				Application Number	10/669,217
				Filing Date	September 23, 2003
				First Named Inventor	Robert W. ESMOND
				Art Unit	1618
				Examiner Name	Vickie Y. Kim
Sheet	6	of	6	Attorney Docket Number	4012.0373-02000

10		van Weeren et al., "Essential role for protein kinase B (PKB) in insulin-induced glycogen synthase kinase 3 inactivation. Characterization and dominant-negative mutant of PKB," <i>J. Biol. Chem.</i> , 273: 13150-13156 (1998).	
		Vekrellis et al., "Neurons regulate extracellular levels of amyloid $\beta$ -protein via proteolysis by insulin-degrading enzyme," <i>J. Neurosci.</i> , 20: 1657-1665 (2000).	
		Virkamäki et al., "Protein-protein interaction in insulin signaling and the molecular mechanisms of insulin resistance," <i>J. Clin. Invest.</i> , 103: 931-943 (1999).	
		White et al., "Insulin rapidly stimulates tyrosine phosphorylation of a $M_r$ 185,000 protein in intact cells," <i>Nature</i> , 318: 183-186 (1985).	
		Wozniak et al., "The cellular and physiological actions of insulin in the central nervous system," <i>Neurochem. Int.</i> , 22: 1-10 (1993).	
		Ye et al., "In vivo actions of insulin-like growth factor-I (IGF-I) on cerebellum development in transgenic mice: evidence that IGF-I increases proliferation of granule cell progenitors," <i>Dev. Brain Res.</i> , 95: 44-54 (1996).	
		Ye et al., "Regulation of insulin-like growth factor I (IGF-I) gene expression in brain of transgenic mice expressing an IGF-I-luciferase fusion gene," <i>Endocrinology</i> , 138: 5466-5475 (1997).	
		Zheng et al., "Insulin-like growth factor-1 (IGF-1): a neuroprotective trophic factor acting via the Akt kinase pathway," <i>J. Neural Transm. Suppl.</i> 261-272 (2000).	

Examiner Signature		Date Considered	2/1/06
--------------------	---	-----------------	--------

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.